

IN THE CLAIMS:

Please substitute the following listing of claims for the previous listing of claims.

1. (Currently amended) A ~~stable~~ respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microstructures, the perforated microstructures comprising at least one bioactive agent wherein said suspension medium comprises at least one propellant and ~~substantially~~ permeates said perforated microstructures.
2. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1, wherein said propellant comprises a compound selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoro-n-propane, perfluoroethane, monochlorodifluoromethane, 1,1-difluoroethane and combinations thereof.
3. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said propellant is a hydrofluoroalkane propellant.
4. (Currently amended) The ~~stable stable~~ respiratory dispersion of claim 3 wherein said hydrofluoroalkane propellant comprises 1,1,1,2-tetrafluoroethane.
5. (Currently amended) The ~~stable~~ respiratory dispersion of claim 3 wherein said hydrofluoroalkane propellant comprises 1,1,1,2,3,3,3-heptafluoro-n-propane.
6. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said perforated microstructures comprise a surfactant.

7. (Currently amended) The ~~stable~~ respiratory dispersion of claim 6 wherein said surfactant is selected from the group consisting of phospholipids, nonionic detergents, nonionic block copolymers, ionic surfactants, biocompatible fluorinated surfactants and combinations thereof.
8. (Cancelled)
9. (Currently amended) The ~~stable~~ dispersion of claim 6 wherein said perforated microstructures comprise oleic acid or its alkali salt.
10. (Currently amended) The ~~stable~~ respiratory dispersion of claim 6 wherein said surfactant comprises a lipid.
11. (Currently amended) The ~~stable~~ respiratory dispersion of claim 10 wherein said lipid has a gel to liquid crystal phase transition greater than about 40°C.
12. (Currently amended) The ~~stable~~ respiratory dispersion of claim 10 wherein said lipid is a phospholipid.
13. (Currently amended) The ~~stable~~ respiratory dispersion of claim 12 wherein said phospholipid is selected from the group consisting of dilauroylphosphatidylcholine, ~~dioleoylphosphatidylcholine~~ dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, distearylphosphatidylcholine, behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof.
14. (Currently amended) The ~~stable~~ respiratory dispersion of claim 6 wherein said perforated microstructures comprise greater than about 10% w/w surfactant.
15. (Currently amended) The ~~stable~~ respiratory dispersion of claim 14 wherein said surfactant comprises a phospholipid.

16. (Currently amended) The ~~stable~~ respiratory dispersion of claim 14 wherein said surfactant comprises oleic acid or its alkali salt.

17. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.4.

18. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.3.

19. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said perforated microstructures comprise hollow porous microspheres.

20. (Currently amended) The ~~stable~~ respiratory dispersion of claim 19 wherein the microspheres comprise a surfactant.

21. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 μm .

22. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein the perforated microstructures comprise a mean geometric diameter that is between 0.5 and 5 μm .

23. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 3 μm .

24. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said bioactive agent has a fine particle fraction following aerosolization of greater than 30%.

25. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said bioactive agent has a fine particle fraction following aerosolization of greater than 50%.

26. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein the density of the suspended particles permeated with the suspension medium substantially matches that of the suspension medium.

27. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said bioactive agent is selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics anticholinergics, anesthetics, anti-tuberculars, imaging agents, cardiovascular agents, enzymes, steroids, genetic material, viral vectors, antisense agents, proteins, peptides and combinations thereof.

28. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of steroids, bronchodilators and peptides.

29. (Currently amended) The ~~stable~~ respiratory dispersion of claim 1 wherein said bioactive agents are selected from the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol and DNase.

30 - 132. (Cancelled)

133. (Currently Amended) A respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microparticles, the perforated microstructures comprising greater than about 20% w/w surfactant and at least one bioactive agent wherein said suspension medium comprises at least one propellant and permeates the perforated microstructures.

134. (Original) The respiratory dispersion of claim 133 wherein said dispersed microparticles comprise greater than about 30% w/w surfactant.

135. (Original) The respiratory dispersion of claim 133, wherein said propellant comprises a compound selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3- heptafluoro-n-propane, perfluoroethane, monochlorodifluoromethane, 1, 1-difluoroethane and combinations thereof.

136. (Original) The respiratory dispersion of claim 133 wherein said propellant is a hydrofluoroalkane propellant.

137. (Original) The respiratory dispersion of claim 136 wherein said hydrofluoroalkane propellant comprises 1,1,1,2-tetrafluoroethane.

138. (Original) The respiratory dispersion of claim 133 wherein said surfactant is selected from the group consisting of phospholipids, nonionic detergents, nonionic block copolymers, ionic surfactants, biocompatible fluorinated surfactants and combinations thereof.

139. (Cancelled.)

NK.56.11
Application No: 10/844,265
Page 7 of 26

140. (Original) The respiratory dispersion of claim 133 wherein said perforated microstructures comprise oleic acid or its alkali salt.

141. (Original) The respiratory dispersion of claim 133 wherein said surfactant comprises a lipid.

142. (Original) The respiratory dispersion of claim 141 wherein said lipid has a gel to liquid crystal phase transition greater than about 40°C.

143. (Original) The respiratory dispersion of claim 141 wherein said lipid is a phospholipid.

144. (Currently Amended) The respiratory dispersion of claim 143 wherein said phospholipid is selected from the group consisting of dilauroylphosphatidylcholine, ~~dioleoylphosphatidylcholine~~, ~~dioleoylphosphatidylcholine~~, dipalmitoylphosphatidylcholine, distearylphosphatidylcholine, behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof.

145. (Original) The respiratory dispersion of claim 133 wherein said microparticles comprise perforated microstructures.

146. (Original) The respiratory dispersion of claim 145 wherein said perforated microstructures comprise hollow porous microspheres.

147. (Original) The respiratory dispersion of claim 146 wherein said hollow porous micro spheres have a mean aerodynamic diameter between about 0.5 to 5 µm.

148. (Currently amended) The respiratory dispersion of claim 133 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 µm.

NK.56.11
Application No: 10/644,265
Page 8 of 26

149. (Original) The respiratory dispersion of claim 133 wherein said bioactive agent is selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, ~~anticholinergics~~ anticholinergics, anesthetics, anti-tuberculars, imaging agents, cardiovascular agents, enzymes, steroids, genetic material, viral vectors, antisense agents, proteins, peptides and combinations thereof.

150. (New) The ~~stable~~ respiratory dispersion of claim 133 wherein said bioactive agents are selected from the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol and DNase.

151. (New) A respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microstructures, the perforated microstructures comprising a structural matrix of phospholipid and at least one bioactive agent, wherein said suspension medium comprises at least one propellant and permeates said perforated microstructures.

152. (New) The respiratory dispersion of claim 151, wherein said propellant comprises a compound selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoro-n-propane, perfluoroethane, monochlorodifluoromethane, 1,1-difluoroethane and combinations thereof.

153. (New) The respiratory dispersion of claim 151 wherein said propellant is a hydrofluoroalkane propellant.

154. (New) The respiratory dispersion of claim 153 wherein said hydrofluoroalkane propellant comprises 1,1,1,2-tetrafluoroethane.

155. (New) The respiratory dispersion of claim 153 wherein said hydrofluoroalkane propellant comprises 1,1,1,2,3,3,3-heptafluoro-n-propane.

156. (New) The respiratory dispersion of claim 151 wherein said perforated microstructures comprise a surfactant.

157. (New) The respiratory dispersion of claim 156 wherein said surfactant is selected from the group consisting of phospholipids, nonionic detergents, nonionic block copolymers, ionic surfactants, biocompatible fluorinated surfactants and combinations thereof.

158. (New) The respiratory dispersion of claim 156 wherein said perforated microstructures comprise oleic acid or its alkali salt.

159. (New) The respiratory dispersion of claim 156 wherein said surfactant comprises a lipid.

160. (New) The respiratory dispersion of claim 151 wherein said phospholipid has a gel to liquid crystal phase transition greater than about 40°C.

161. (New) The respiratory dispersion of claim 151 wherein said phospholipid is selected from the group consisting of dilauroylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, distearylphosphatidylcholine behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof.

162. (New) The respiratory dispersion of claim 151 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.4.

163. (New) The respiratory dispersion of claim 151 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.3.

164. (New) The respiratory dispersion of claim 151 wherein said perforated microstructures comprise hollow porous microspheres.

165. (New) The respiratory dispersion of claim 151 wherein the perforated microspheres comprise calcium.

166. (New) The respiratory dispersion of claim 151 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 μm .

167. (New) The respiratory dispersion of claim 151 wherein the perforated microstructures comprise a mean geometric diameter that is between 0.5 and 5 μm .

168. (New) The respiratory dispersion of claim 151 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 3 μm .

169. (New) The respiratory dispersion of claim 151 wherein said bioactive agent has a fine particle fraction following aerosolization of greater than 30%.

170. (New) The respiratory dispersion of claim 151 wherein the density of the suspended particles permeated with the suspension medium substantially matches that of the suspension medium.

171. (New) The respiratory dispersion of claim 151 wherein said bioactive agent is selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics, anesthetics, anti-tuberculars, imaging agents, cardiovascular agents, enzymes, steroids, genetic material, viral vectors, antisense agents, proteins, peptides and combinations thereof.

172. (New) The respiratory dispersion of claim 151 wherein said bioactive agents are selected from the group consisting of steroids, bronchodilators and peptides.

173. (New) The respiratory dispersion of claim 151 wherein said bioactive agents are selected from the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol and DNase.

174. (New) A respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microstructures, the perforated microstructures comprising a structural matrix of phospholipid, calcium, and at least one bioactive agent, wherein said suspension medium comprises at least one propellant and permeates said perforated microstructures.

175. (New) The respiratory dispersion of claim 174 wherein said propellant comprises a compound selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoro-n-propane, perfluoroethane, monochlorodifluoromethane, 1,1-difluoroethane and combinations thereof.

176. (New) The respiratory dispersion of claim 174 wherein said propellant is a hydrofluoroalkane propellant.

177. (New) The respiratory dispersion of claim 176 wherein said hydrofluoroalkane propellant comprises 1,1,1,2-tetrafluoroethane.

178. (New) The respiratory dispersion of claim 176 wherein said hydrofluoroalkane propellant comprises 1,1,1,2,3,3,3-heptafluoro-n-propane.

179. (New) The respiratory dispersion of claim 174 wherein said perforated microstructures comprise a surfactant.

180. (New) The respiratory dispersion of claim 179 wherein said surfactant is selected from the group consisting of phospholipids, nonionic detergents, nonionic block copolymers, ionic surfactants, biocompatible fluorinated surfactants and combinations thereof.

181. (New) The respiratory dispersion of claim 179 wherein said perforated microstructures comprise oleic acid or its alkali salt.

182. (New) The respiratory dispersion of claim 179 wherein said surfactant comprises a lipid.

183. (New) The respiratory dispersion of claim 174 wherein said phospholipid has a gel to liquid crystal phase transition greater than about 40°C.

184. (New) The respiratory dispersion of claim 174 wherein said phospholipid is selected from the group consisting of dilauroylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteoylphosphatidylcholine behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof.

185. (New) The respiratory dispersion of claim 174 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.4.

186. (New) The respiratory dispersion of claim 174 wherein said suspension medium and said perforated microstructures have a refractive index differential of less than about 0.3.

187. (New) The respiratory dispersion of claim 174 wherein said perforated microstructures comprise hollow porous microspheres.

188. (New) The respiratory dispersion of claim 174 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 μm .

189. (New) The respiratory dispersion of claim 174 wherein the perforated microstructures comprise a mean geometric diameter that is between 0.5 and 5 μm .

190. (New) The respiratory dispersion of claim 174 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 3 μm .

191. (New) The respiratory dispersion of claim 174 wherein said bioactive agent has a fine particle fraction following aerosolization of greater than 30%.

192. (New) The respiratory dispersion of claim 174 wherein the density of the suspended particles permeated with the suspension medium substantially matches that of the suspension medium.

193. (New) The respiratory dispersion of claim 174 wherein said bioactive agent is selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics, anesthetics, anti-tuberculars, imaging agents, cardiovascular agents, enzymes, steroids, genetic material, viral vectors, antisense agents, proteins, peptides and combinations thereof.

194. (New) The respiratory dispersion of claim 174 wherein said bioactive agents are selected from the group consisting of steroids, bronchodilators and peptides.

195. (New) The respiratory dispersion of claim 174 wherein said bioactive agents are selected from the group consisting of budesonide, fluticasone propionate, salmeterol, formoterol and DNase.

196. (New) A respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microstructures, the suspension medium comprising at least one propellant that permeates said perforated microstructures, and the perforated microstructures comprising at least one bioactive agent in a structural matrix comprising at least one phospholipid selected from the group consisting of dilauroylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteoylphosphatidylcholine, behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof.

197. (New) The respiratory dispersion of claim 196 wherein the perforated microspheres comprise calcium.

198. (New) The respiratory dispersion of claim 196 wherein the perforated microspheres comprise magnesium.

199. (New) The respiratory dispersion of claim 196 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 μm .

200. (New) The respiratory dispersion of claim 196 wherein the perforated microstructures comprise a mean geometric diameter that is between 0.5 and 5 μm .

201. (New) The respiratory dispersion of claim 196 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 3 μm .

202. (New) A respiratory dispersion for the pulmonary delivery of one or more bioactive agents, the dispersion comprising a suspension medium having dispersed therein a plurality of perforated microstructures, the suspension medium comprising at least one propellant that permeates said perforated microstructures, and the perforated microstructures comprising:

a structural matrix comprising at least one phospholipid selected from the group consisting of dilauroylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine, distearylphosphatidylcholine, behenoylphosphatidylcholine, arachidoylphosphatidylcholine and combinations thereof; and

at least one bioactive agent selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics, anesthetics, anti-tuberculars, imaging agents, cardiovascular agents, enzymes, steroids, genetic material, viral vectors, antisense agents, proteins, peptides and combinations thereof.

203. (New) The respiratory dispersion of claim 202 wherein the perforated microspheres comprise calcium.

204. (New) The respiratory dispersion of claim 202 wherein the perforated microspheres comprise magnesium.

NK.56.11
Application No: 10/644,265
Page 18 of 26

205. (New) The respiratory dispersion of claim 202 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 5 μm .

206. (New) The respiratory dispersion of claim 202 wherein the perforated microstructures comprise a mean geometric diameter that is between 0.5 and 5 μm .

207. (New) The respiratory dispersion of claim 202 wherein the perforated microstructures comprise a mean geometric diameter that is between 1 and 3 μm .